Phentermine/Topiramate (QSYMIA)

Criteria for Use

April 2013

VA Pharmacy Benefits Management Services, Medical Advisory Panel, and VISN Pharmacist Executives

The following recommendations are based on medical evidence, clinician input, and expert opinion. The content of the document is dynamic and will be revised as new information becomes available. The purpose of this document is to assist practitioners in clinical decision-making, to standardize and improve the quality of patient care, and to promote cost-effective drug prescribing. **THE CLINICIAN SHOULD UTILIZE THIS GUIDANCE AND INTERPRET IT IN THE CLINICAL CONTEXT OF THE INDIVIDUAL PATIENT. INDIVIDUAL CASES THAT ARE EXCEPTIONS TO THE EXCLUSION AND INCLUSION CRITERIA SHOULD BE ADJUDICATED AT THE LOCAL FACILITY ACCORDING TO THE POLICY AND PROCEDURES OF ITS P&T COMMITTEE AND PHARMACY SERVICES.**

The Product Information should be consulted for detailed prescribing information.

See the VA National PBM-MAP-VPE Monograph on this drug at www.pbm.va.gov or http://vaww.pbm.va.gov for further information.

Exclusion Criteria *If the answer to ANY item below is met, then the patient should NOT receive phentermine/topiramate.*

☐ Pregnancy (Category X; i.e., known pregnancy or positive pregnancy test)
☐ Glaucoma
☐ Hyperthyroidism
☐ The patient has had a recent (within the past 6 months) cardiac or cerebrovascular event, or unstable angina
☐ The patient has end stage renal disease on dialysis
☐ The patient has severe hepatic impairment (Child-Pugh 10-15)
☐ History of cholelithiasis in the past 6 months
☐ History of nephrolithiasis
☐ Previous bariatric surgery
☐ History of recurrent major depression, presence or history of suicidal behavior or ideation with intent to act or current substantial depressive symptoms (e.g. a PHQ-9 $\geq$10)
☐ Use of a monoamine oxidase inhibitor (MAOI) in the past 14 days
☐ Known hypersensitivity or idiosyncrasy to the sympathomimetic amines, phentermine, or topiramate.
☐ The patient is taking another weight loss medication (concurrently), e.g., orlistat, phentermine, or lorcaserin, or a stimulant, e.g., amphetamine, methylphenidate, or modafinil.
☐ Concomitant use of an oral carbonic anhydrase inhibitor
☐ The patient is taking topiramate more than100 mg/day for another condition, e.g., seizures, migraine headache.

Inclusion Criteria *The answers to all of the following must be fulfilled in order to meet criteria.*

☐ The patient is enrolled and has been an active participant in a MOVE!® program for at least 3 months
☐ The patient's weight has plateaued on diet, exercise, behavioral or other interventions
☐ The provider has completed training provided by the Risk Evaluation and Mitigation Strategy (REMS) program for phentermine/topiramate (See Issues for Consideration)
☐ For patients taking topiramate 100 mg or less per day for another condition (e.g., seizure disorder, migraine headache), the dose of topiramate is lowered so the cumulative dose does not exceed 100 mg/day. (See Issues for consideration)

☐ The patient's BMI is greater than or equal to 30 kg/m2 **OR**
☐ The patient's BMI is greater than or equal to 27 kg/m2 in the presence of at least one weight-related comorbidity such as hypertension, type 2 diabetes mellitus, dyslipidemia, metabolic syndrome, obstructive sleep apnea, or degenerative joint disease (osteoarthritis).

☐ For women of reproductive potential, obtain negative pregnancy test before starting treatment and monthly tests thereafter (See Issues for Consideration). The patient is provided counseling on the importance of consistent use of effective methods of contraception and the potential risk vs. benefit of taking phentermine/topiramate as provided in the REMS program.

Renewal Criteria *All must be met*

☐ The patient has attended follow-up appointments. Initial follow-up is to be in 2 to 4 weeks after starting phentermine/topiramate, then monthly for 3 months. The patient is to be weighed at each follow-up visit.
☐ The patient has achieved the weight loss goals at 12 and/or 24 weeks as specified under Dosage and Administration. See Issues for Consideration for additional clarification.
☐ For women of childbearing potential, monthly negative pregnancy test has been reported and recorded in the patient's medical record per local requirements. See Issues for Consideration
☐ The patient is not experiencing intolerable side effects.
☐ The patient wishes to continue phentermine/topiramate.
☐ The patient has no contraindications to phentermine/topiramate including hypersensitivity or the development of kidney stones, uncorrectable hypokalemia or metabolic acidosis.

Criteria for Refills every 6 months (after initial 12 and/or 24 week refill(s))
☐ The patient has maintained 67% of their initial weight loss or >5% loss of their baseline total body weight to date or has continued to lose weight
AND
☐ The patient's BMI is ≥24 kg/m^2

Dosage and Administration

Dose Titration

- One phentermine 3.75 mg/topiramate 23 mg extended-release capsule in each morning for 14 days; then increase to 7.5 mg/46 mg each morning for an additional 12 weeks.
- If a weight loss of 3% of baseline body weight is not achieved after 12 weeks, then increase the dose to 11.25 mg/69 mg each morning for 14 days; then increased to 15 mg/92 mg (maximum dose) each daily.
- If after 12 weeks on 15 mg/92 mg the patient has not lost at least 5% of baseline body weight, discontinue phenteramine/topiramate, as it is unlikely that the patient will achieve and sustain clinically meaningful weight loss with continued treatment.
- The 3.25 mg/23 mg and 11.25 mg/69 mg formulations are for titration purposes only.
- Discontinuation of phentermine 15 mg/ topiramate 92 mg gradually by taking a dose every other day for at least 1 week prior to stopping the medication altogether, due to the possibility of precipitating a seizure.

The dose for patients with moderate-severe renal impairment (CrCl <50 mL/min) or with moderate hepatic impairment (Child-Pugh score 5-6) should not exceed 7.5 mg/46 mg once daily.

Monitoring

- Weight
- Blood pressure (orthostatic) and/or signs/symptoms of hypotension in patients taking antihypertensives or other medications that can lower blood pressure
- Resting heart rate
- Serum bicarbonate, especially if patient is taking another carbonic anhydrase inhibitor
- Serum potassium, especially if patient is taking another carbonic anhydrase inhibitor
- Glucose and/or signs/symptoms of hypoglycemia in patients with diabetes
- Mood (symptoms of depression) and sleep disorders
- Pregnancy tests in women of reproductive potential

Issues for Consideration

- The phentermine/topiramate combination has not been studied in patients with heart failure and should be used with caution in these patients. Monitor heart failure patients for changes in heart rate as well as signs and symptoms of heart failure.
- Persons 65 years of age older accounted for 7% of subjects in clinical trials with phentermine/topiramate. No differences in efficacy or safety were observed in older compared to younger study participants. However, given insufficient representation of persons 65 years and older, caution is advised with dose titration, response and monitoring.
- Patients taking <100mg of topiramate for other indications such as seizure disorder or migraine headache should have their topiramate dose adjusted during dosage titration of phentermine/topiramate and during maintenance dosing so that their total topiramate concentration does not exceed 100 mg.
- Phentermine/topiramate is subject to a Risk Evaluation and Mitigation Strategy (REMS). Online prescriber training can be accessed at http://www.qsymiarems.com/
- In the clinical trials, phentermine/topiramate was started simultaneously with nonpharmacologic interventions including diet, exercise and behavioral modification. These criteria for use require the patient's weight to have plateaued with these interventions prior to starting phentermine/topiramate. Given this difference, it is unknown if a 3% weight loss 12 weeks after starting phentermine 7.5 mg/topiramate 46 mg is an achievable goal, thus additional flexibility in goal or achieving goal may be necessary before increasing the dose. This same approach may be necessary when evaluating the extent of weight loss after 12 weeks of phentermine 15 mg/topiramate 92 mg.
- Pregnancy Testing
    - The prescribing information for phentermine/topiramate states under Warnings and Precautions that "*women of reproductive potential obtain a negative pregnancy test before treatment and monthly thereafter and that they use effective contraception*." The Healthcare Provider Counseling Tool for Females of Reproductive Potential provided by the REMS program states "*pregnancy testing is*

recommended before initiating treatment with Qsymia and monthly during treatment" and that the provider "Advise patients to undergo pregnancy testing before starting treatment with Qsymia and monthly thereafter. Discuss with patients whether pregnancy testing should be performed in the office or with a home pregnancy test."

  - The REMS program does not require or provide a mechanism for the pregnancy test results to be reported to the certified pharmacy prior to dispensing phentermine/topiramate.
  - The provision of pregnancy testing by VA Laboratory Services is the most reliable mechanism.
  - Each individual facility is to have a mechanism in place to ensure monthly pregnancy testing is performed in women of child bearing potential taking phentermine/topiramate. The process of obtaining and documenting pregnancy testing and the results are to be determined by the VA facility or VISN from which the Veteran receives care.
- The mechanism by which the Veteran initially obtains and refills phentermine/topiramate from the certified dispensing pharmacy is to be determined by the VA facility or VISN from which the Veteran receives care provided it is consistent with procedures agreed upon by the VA and the certified pharmacy, and the Specialty Pharmacy Prescription Documentation Procedures (both available at https://vaww.cmopnational.va.gov/cmop/PBM/Special%20Handling%20Drugs/Forms/AllItems.aspx.

Prepared: April 2013. Contact: Todd Semla, MS, Pharm.D., VA Pharmacy Benefits Management Services